

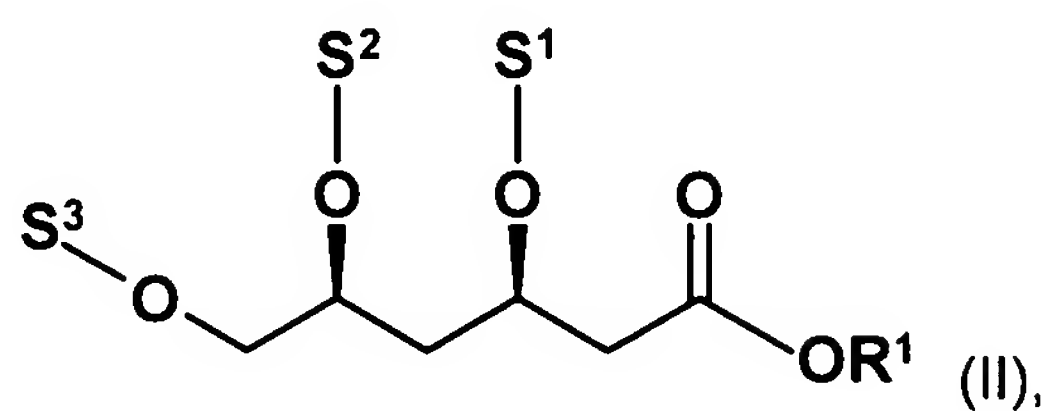
**Patent claims:**

5

1. Process for the preparation of a statin, comprising the following steps:

a) Preparation of a compound of the formula II

10



in which

S<sup>1</sup> denotes a hydrogen atom or a hydroxyl protective group,

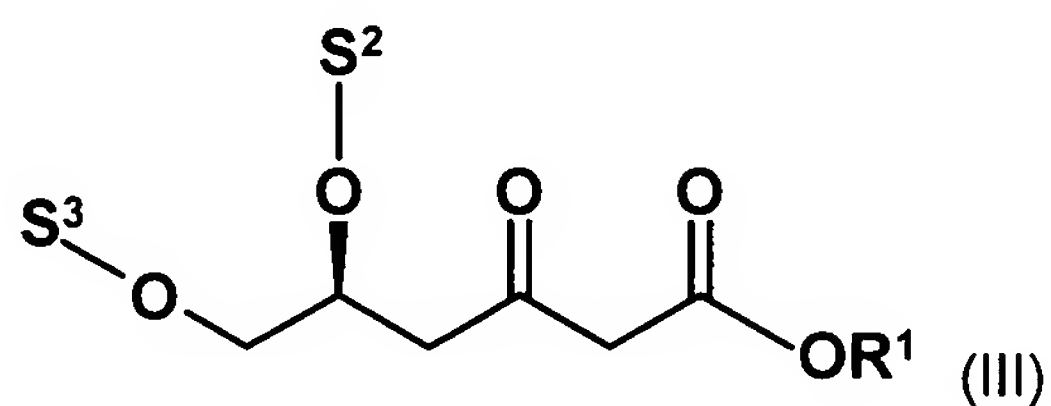
S<sup>2</sup> and S<sup>3</sup>, independently of one another, denote hydroxyl protective groups and

15

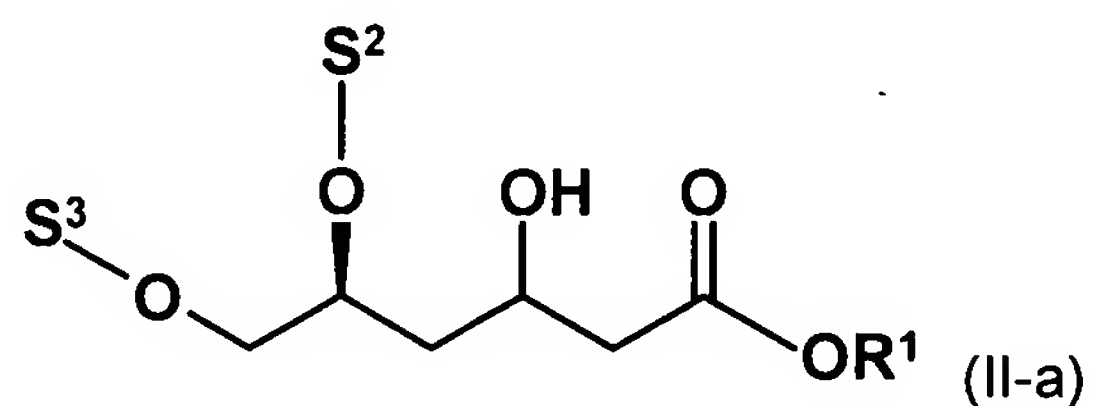
R<sup>1</sup> represents a hydrogen atom or a carboxyl protective group,

by stereoselective hydrogenation of a compound of the formula III

20

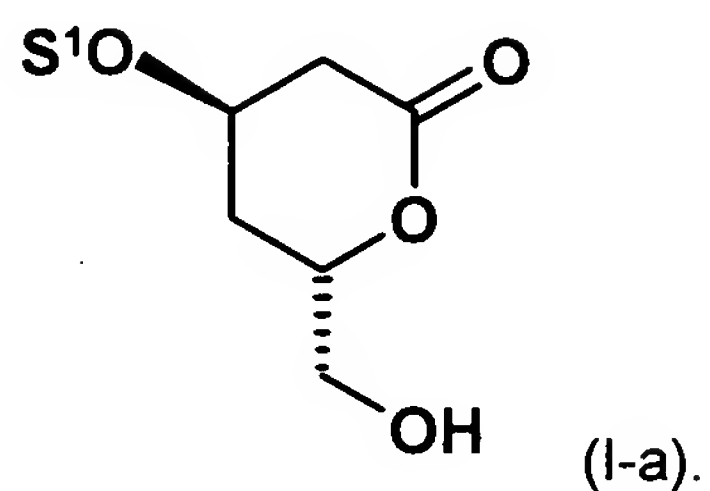


to give a compound of the formula II-a



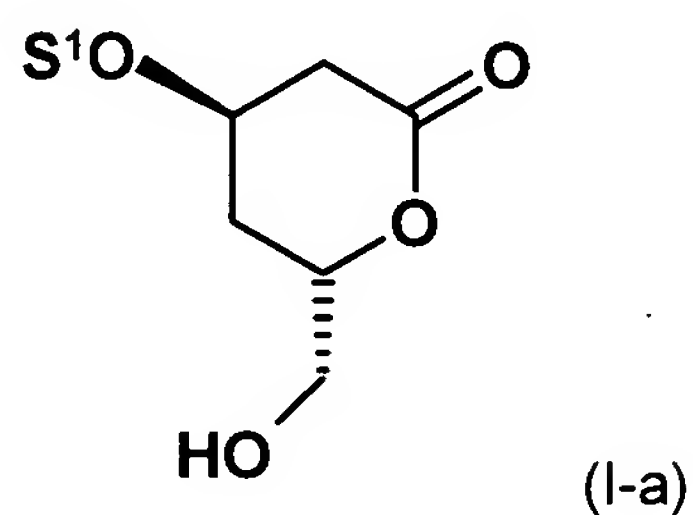
and optionally introduction of a hydroxyl protective group and

- b) lactonization of the compound of the formula II to give a compound of the formula I-a



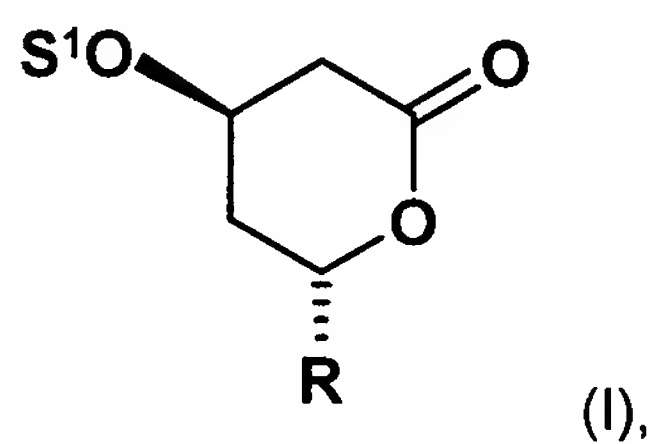
- 5 2. Process according to Claim 1, comprising the further step

- c) conversion of the compound of the formula I-a



10

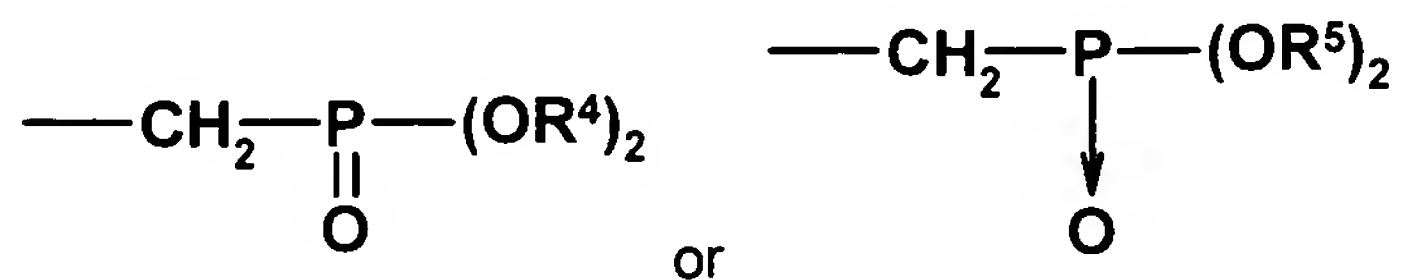
into a compound of the formula I



- 15 where the radical

$S^1$  is as defined in Claim 1,

$R$  denotes  $-CH_2R^2$ ,  $-CHO$ ,  $-CH=P(R^3)_3$ ,  $-CH_2-P^+(R^3)_3M^-$ ,



$R^2$  denotes a halogen atom,  $-C\equiv N$ ,  $-CH_2NH_2$ ,  $-SO_2-R^6$  or a leaving group,

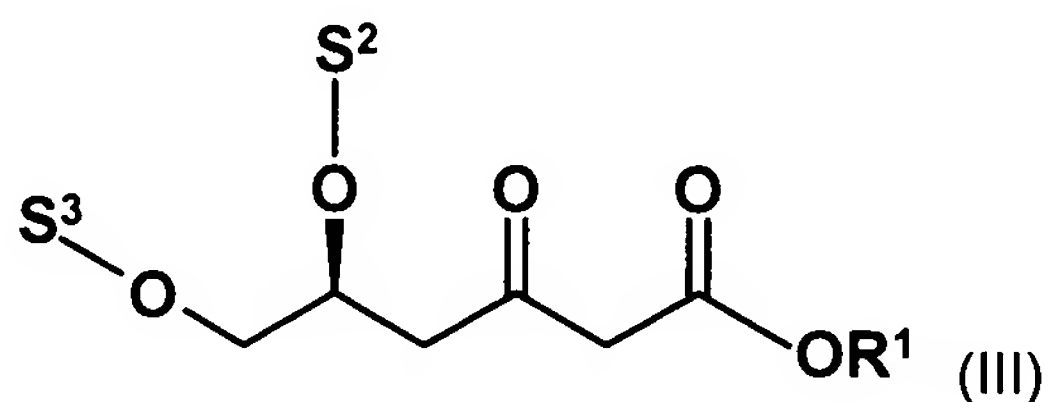
$R^3$ ,  $R^4$  and  $R^5$  complete a Wittig radical or a Horner-Wittig radical,

$R^6$  denotes a hydrogen atom or a  $C_{1-3}$ -alkyl or a  $C_{5-10}$ -aryl radical, which are optionally substituted by one or more radicals which, independently of one another, are selected from halogen atoms, heterocycles which contain 0 to 10 carbon atoms and 1 to 10 heteroatoms selected from sulphur, nitrogen and oxygen atoms, and functional groups and

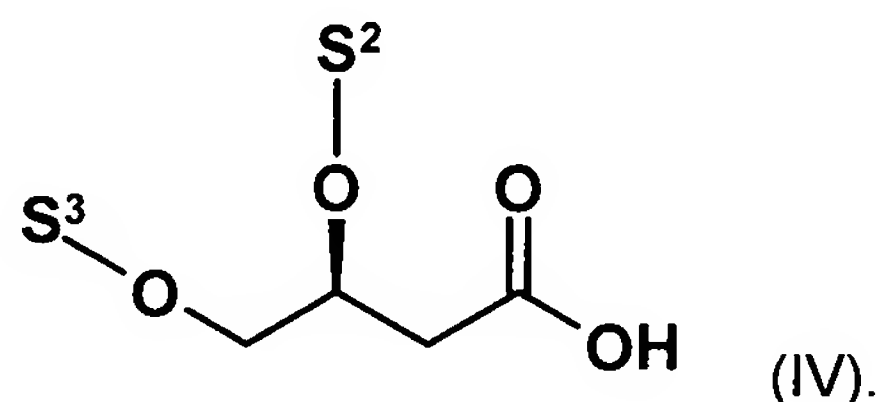
$M^+$  represents an opposite ion.

3. Process according to Claim 1 or 2, comprising the step:

preparation of a compound of the formula III

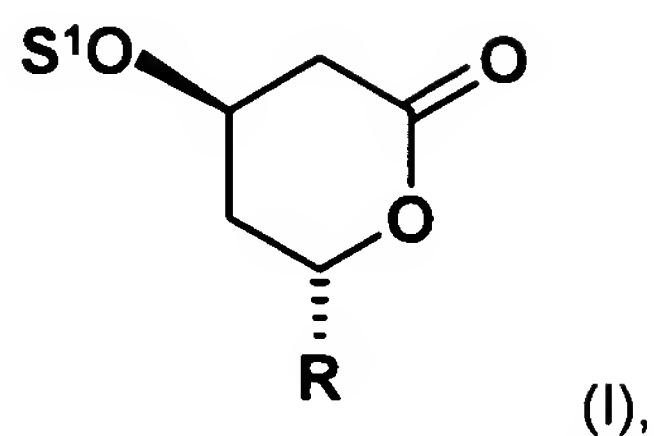


by chain extension of a compound of the formula IV

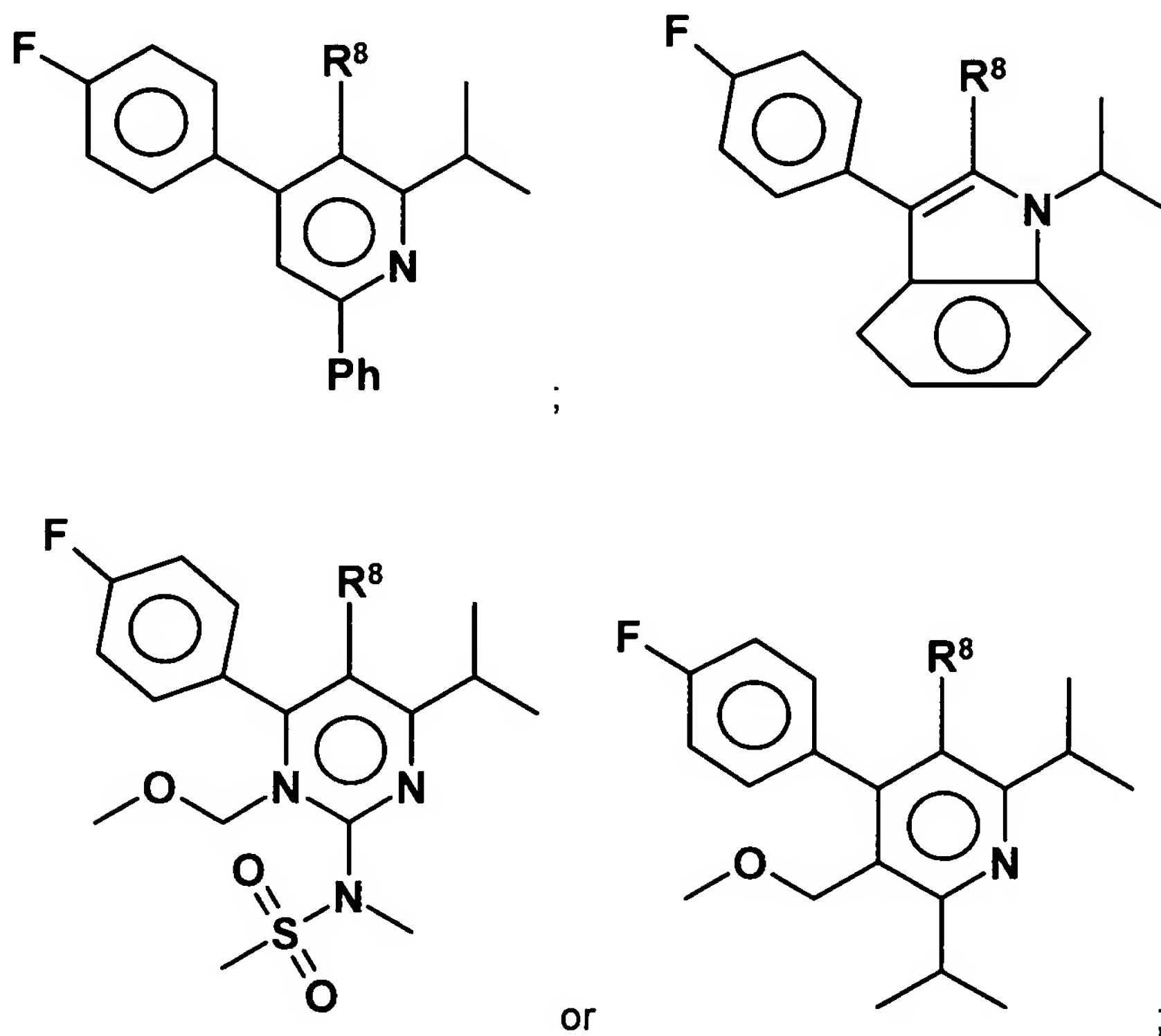


4. Process according to any of Claims 1 to 3, the compound of the formula I being converted into the statin by one of the following process steps and then optionally by opening of the lactone ring and optionally by removal of protective groups:

a) reaction of a compound of the formula (I)

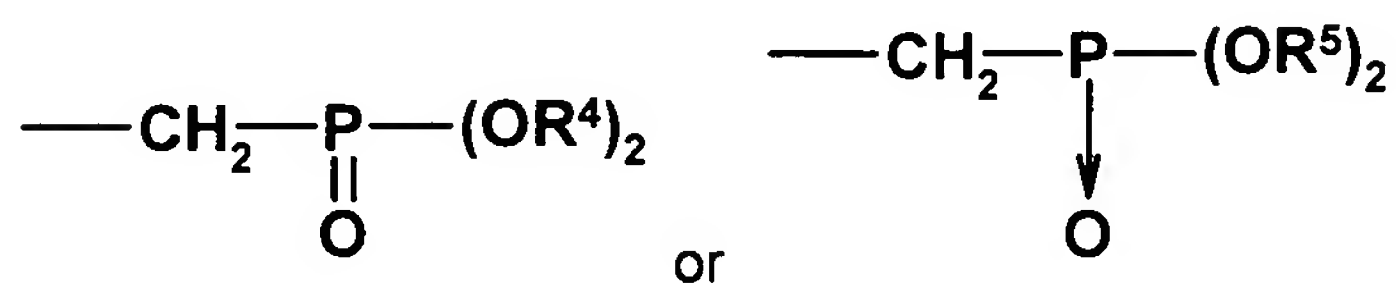


in which the radical R represents a CHO group and the radical S<sup>1</sup> is as defined in Claim 1,  
5 with a compound of the formula



in which

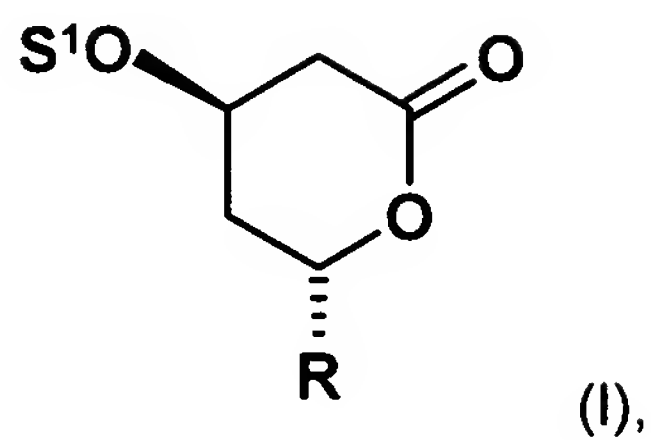
R<sup>8</sup> denotes -CH=P(R<sup>3</sup>)<sub>3</sub>, -CH<sub>2</sub>-P<sup>+</sup>(R<sup>3</sup>)<sub>3</sub>M<sup>-</sup>,



15 where R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and M are as defined in Claim 1,

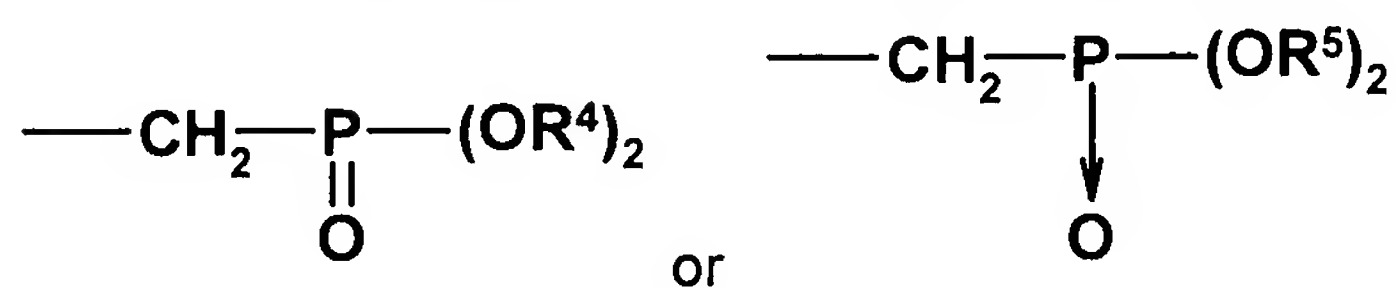
Atty Docket No.: LNK-014

b) reaction of a compound of the formula I



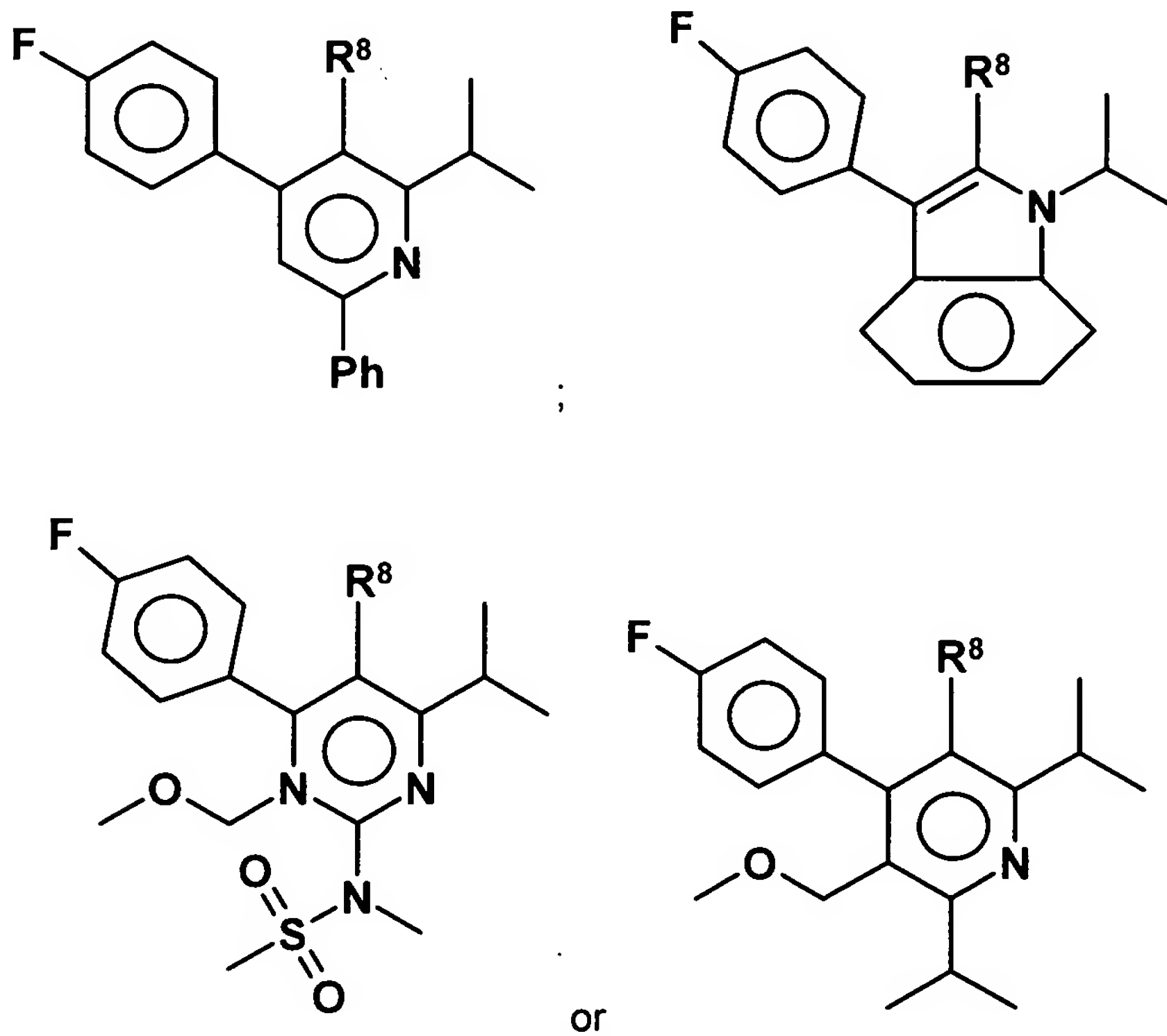
5 in which

the radical R denotes  $-\text{CH}=\text{P}(\text{R}^3)_3$ ,  $-\text{CH}_2-\text{P}^+(\text{R}^3)_3\text{M}^-$ ,



with a compound of the formula

10



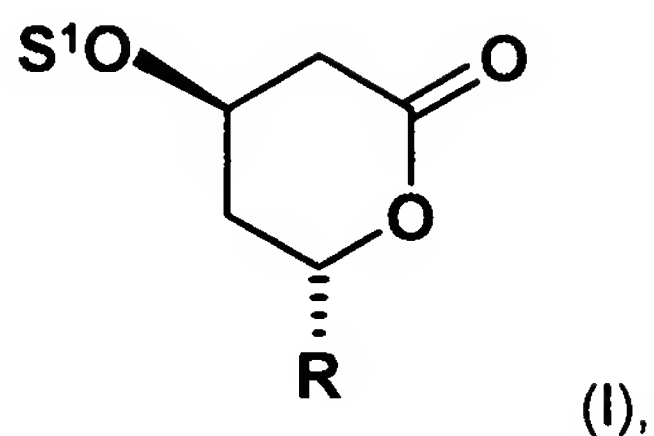
in which

15  $\text{R}^8$  denotes  $-\text{CHO}$ ,

where  $R^3$ ,  $R^4$ ,  $R^5$  and M are as defined in Claim 1,



c) reaction of a compound of the formula I

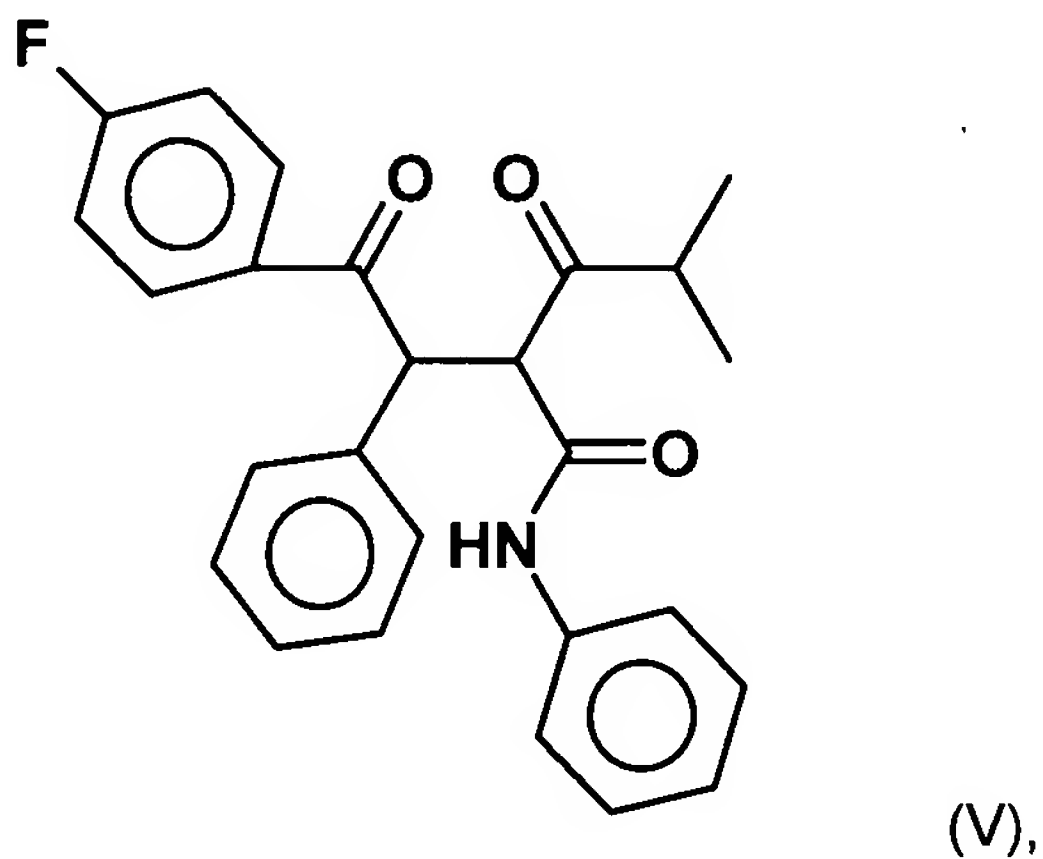


5 in which  
the radical R is a group  $-\text{CH}_2-\text{C}\equiv\text{N}$ ,

Hydrogenation of the compound of the formula I in which the radical R is a group  $-\text{CH}_2-\text{C}\equiv\text{N}$ , to  
give a compound of the formula I in which the radical R is a group  $-\text{CH}_2-\text{CH}_2\text{NH}_2$ ,

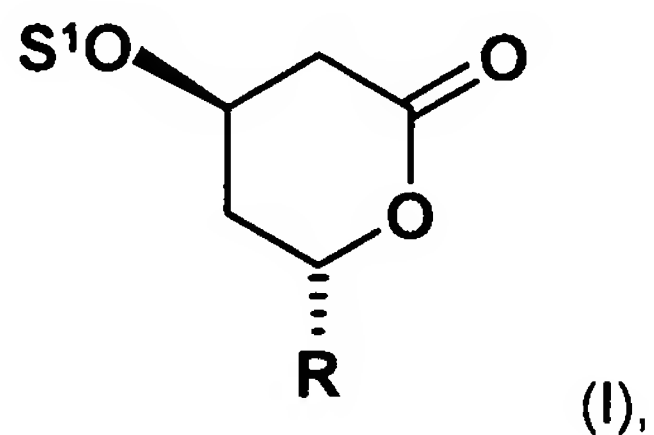
10

and reaction of the compound of the formula I in which the radical R is a group  $-\text{CH}_2-\text{CH}_2\text{NH}_2$   
with a compound of the formula V



15

d) hydrogenation of a compound of the formula I

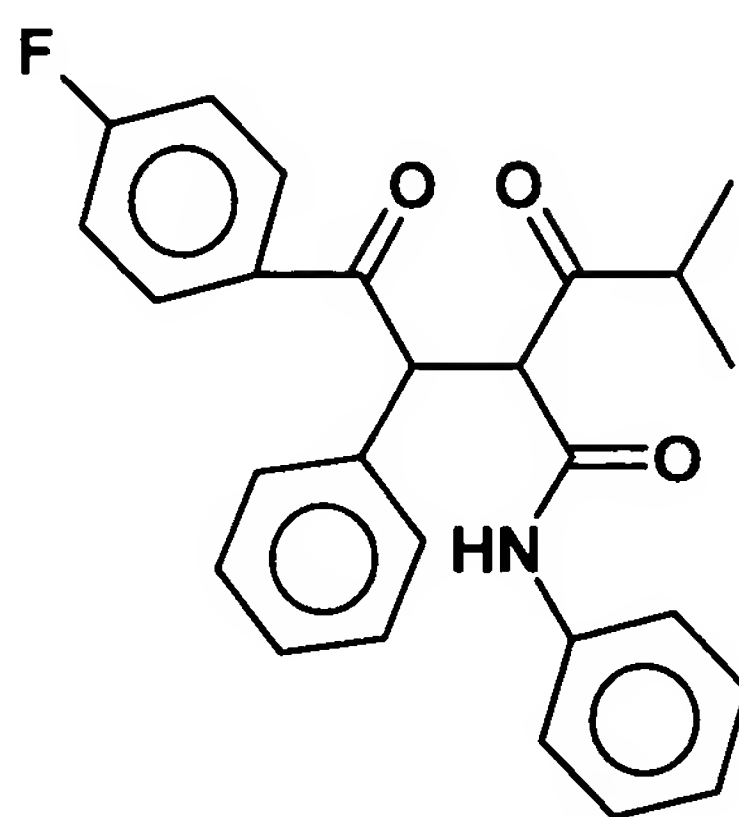


Atty Docket No.: LNK-014

in which

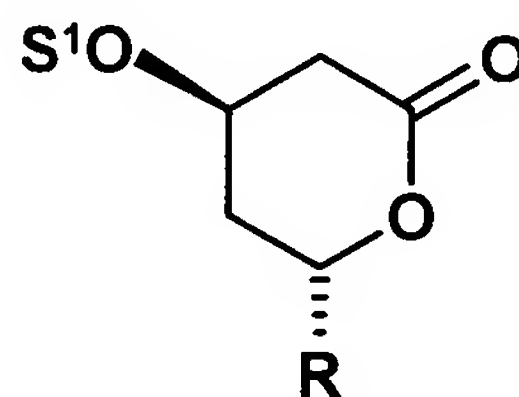
the radical R is a group  $-\text{CH}_2-\text{C}\equiv\text{N}$ , to give a compound of the formula I in which the radical R is a group  $-\text{CH}_2-\text{CH}_2\text{NH}_2$ ,

- 5 and reaction of the compound of the formula I in which the radical R is a group  $-\text{CH}_2-\text{CH}_2\text{NH}_2$  with a compound of the formula V



(V),

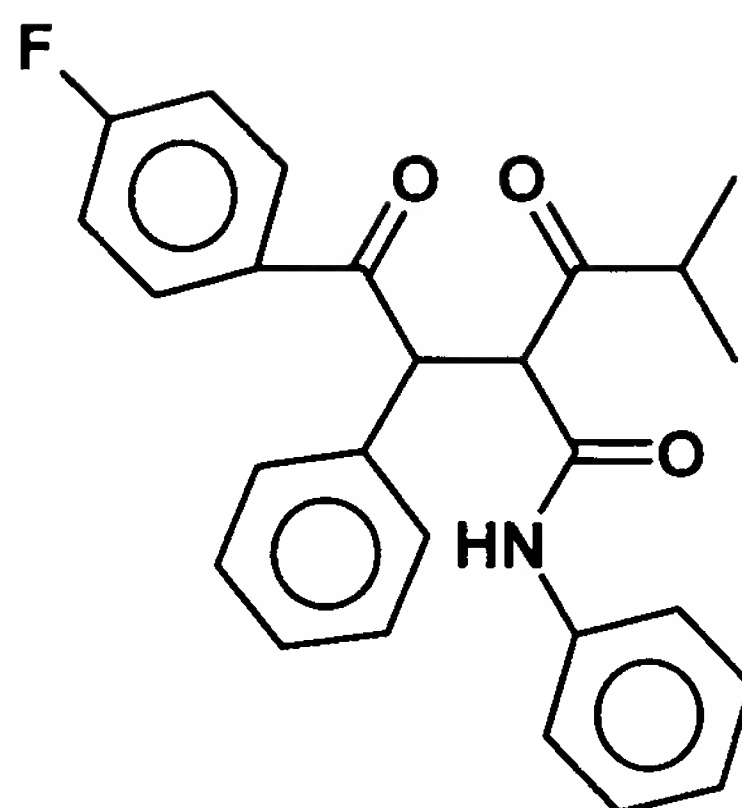
- 10 e) reaction of a compound of the formula (I)



(I),

in which

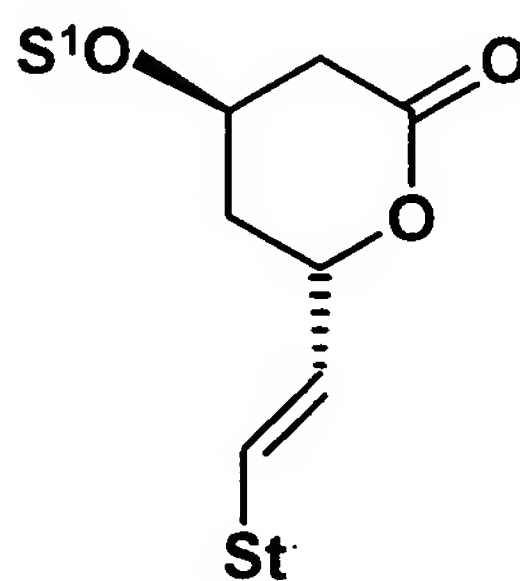
- 15 the radical R is a group  $-\text{CH}_2-\text{CH}_2\text{NH}_2$ , with a compound of the formula V



(V).

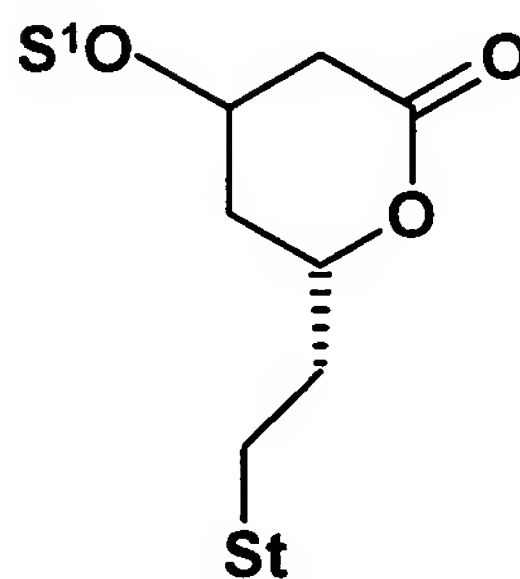
5. Process according any of Claims 1 to 4, characterized in that a compound of the formula

5



in which  $S^1$  is as defined in Claim 1 and St represents the radical of the statin, is converted into a compound of the formula

10



by catalytic hydrogenation, and optionally the protective group  $S^1$  is removed and optionally the lactone ring is opened.

15

6. Process according to any of Claims 1 to 5, the hydroxyl protective group  $S^1$  being selected from a trimethylsilyl, triisopropylsilyl, trimethylsilylethyl, tert-butyldimethylsilyl, tert-butylmethylsilyl, di-tert-butylmethylsilyl, tert-butyldiphenylsilyl, triphenylsilyl, diphenylmethylsilyl, tris(trimethylsilyl) and para-tosyl protective group.

5

7. Process according to any of Claims 1 to 6, the protective groups  $S^2$  and  $S^3$  being bridged.

8. Process according to Claim 7, the protective groups  $S^2$  and  $S^3$  together representing an isopropylidene protective group.

10

9. Process according to any of Claims 2 to 7, the radical R representing a radical  $CH_2R^2$  and  $R^2$  representing a leaving group, the leaving group being selected from a halogen atom and a radical  $-OSO_2-C_1-C_6$ -alkyl or  $-OSO_2-C_5-C_{10}$ -aryl.

15

10. Process according to any of Claims 1 to 9, the radical  $R^1$  denoting a hydrogen atom or a  $C_{1-3}$ -alkyl or  $C_{4-10}$ -aryl radical, which are optionally substituted by one or more radicals, which, independently of one another, are selected from halogen atoms, heterocycles which have 0 to 10 carbon atoms and 1 to 10 heteroatoms selected from sulphur, nitrogen and oxygen atoms, and functional groups.

20

11. Process according to any of Claims 1 to 10,

$R^3$  denoting a  $C_5$ - to  $C_{10}$ -aryl radical which is optionally substituted by one or two  $C_1-C_4$ -alkyl radicals and/or halogen atoms, a  $C_1-C_4$ -alkyl radical or a  $C_5-C_{10}$ -cycloalkyl radical,

25

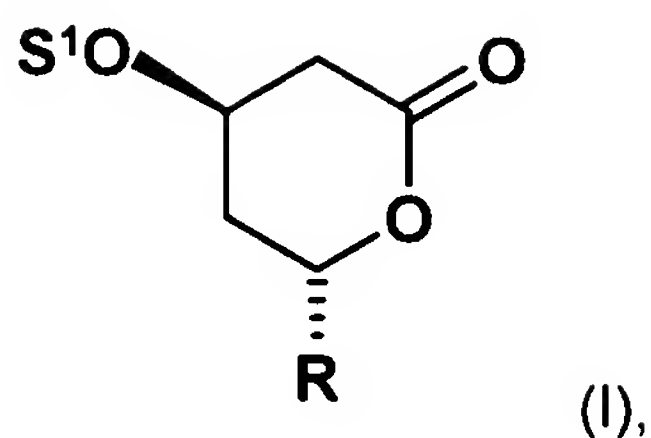
$R^4$  denoting a  $C_1-C_4$ -alkyl radical,

$R^5$  denoting a  $C_1-C_6$ -alkyl or  $C_5-C_{10}$ -aryl radical.

12. Process according to any of Claims 1 to 11, the statin being fluvastatin, rosuvastatin, cerivastatin, glenvastatin or atorvastatin.

30

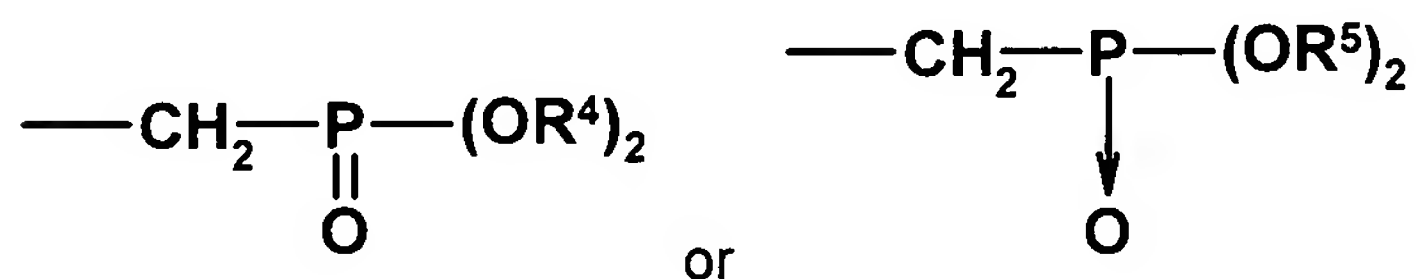
13. Compound of the formula I



in which

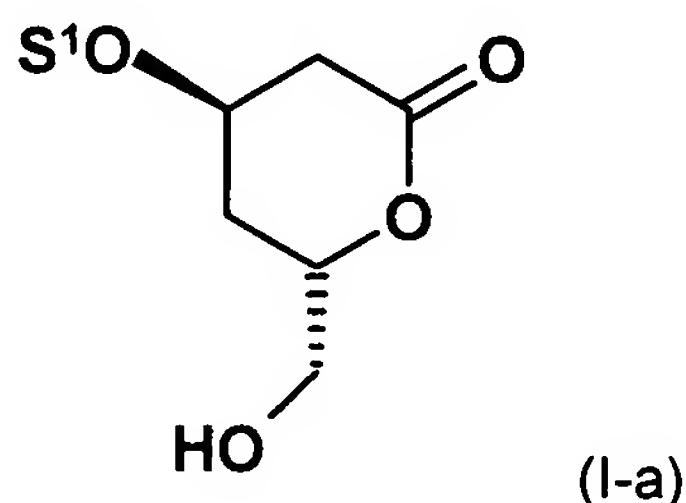
S<sup>1</sup> and R are as defined in Claim 2, with the proviso that the radical S<sup>1</sup> does not represent a  
 5 tert-butyldimethylsilyl group if the radical R represents a CHO, -CH<sub>2</sub>-OTos, -CH<sub>2</sub>Cl or -CH<sub>2</sub>I  
 group.

14. Compound according to Claim 13, in which the radical S<sup>1</sup> represents a tert-  
 butyldimethylsilyl group and the radical R represents a -CH<sub>2</sub>R<sup>2</sup>, -CH=P(R<sup>3</sup>)<sub>3</sub>, -CH<sub>2</sub>-P<sup>+</sup>(R<sup>3</sup>)<sub>3</sub>M<sup>-</sup>,

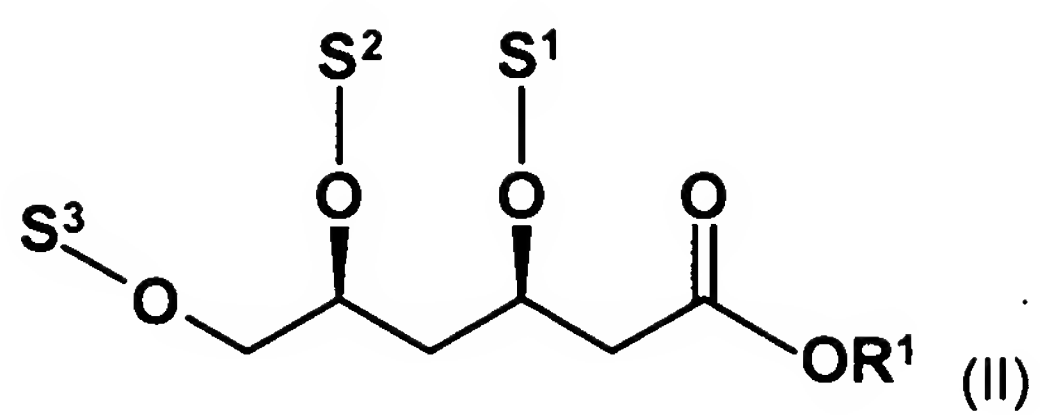


group, where R<sup>2</sup> represents a bromine  
 atom, a -C≡N, a -CH<sub>2</sub>NH<sub>2</sub> group or a radical -SO<sub>2</sub>-R<sup>6</sup>, and R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and M are as defined in  
 Claim 2.

15. Process for the preparation of a compound of a formula (I-a)



in which the radical S<sup>1</sup> is as defined in Claim 1, characterized in that a compound of the formula  
 II



in which

S<sup>1</sup>, S<sup>2</sup>, S<sup>3</sup> and R<sup>1</sup> are as defined in Claim 1, is converted into the compound of the formula I-a

5 by lactonization.